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TECHNICAL NOTE

ELECTRONIC DELOCALIZATION AND
BIOCHEMICAL EVOLUTION

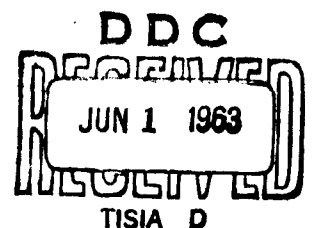
by

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For Research in Atomic, Molecular and Solid-State Theory
Uppsala University, Uppsala, Sweden

November 15, 1962

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TECHNICAL NOTE

ELECTRONIC DELOCALIZATION AND
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*

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In one of his recent books Szent-Gyorgyi ¹⁾ states that "research is to see what everybody has seen and think what nobody has thought". When a quantum chemist, used to think in terms of σ and π electrons, localized and delocalized molecular orbitals, saturated and conjugated compounds, comes for the first time in contact with biochemistry he is bound to be attracted by aspects of this science which escaped the attention of other types of investigators. What struck us as one essential although apparently hitherto unnoticed aspect of biochemistry is the fact that all the essential biomolecules which are related to, or perform, the fundamental functions of the living matter are constituted of completely, or at least partially conjugated (resonating) systems, rich in delocalized π electrons ^{2, 3)}. Thus, the three fundamental structural units of the cell are undoubtedly the nucleic acids, the proteins, and the energy-rich phosphates. Now, the most significant constituents of the nucleic acids which impose upon them their biological personality and determine their specific functions are the purine and pyrimidine bases, which are conjugated heterocycles. In the biologically important energy-rich phosphates, the mobile electrons of the phosphoryl group always interact either with those of another similar phosphoryl group (the case of the pyrophosphates ATP and ADP) or with those of a π electron-possessing organic radical (the case of the guanidino-, acyl- and enolphosphates). No such interaction is present in the energy poor phosphates, in which the phosphoryl group is attached to a saturated carbon. As to the proteins, although they appear, at first sight, to be essentially non-resonating entities containing only isolated conjugated fragments (each peptide link is such a fragment ⁴⁾), there are a number of indications that their over-all supramolecular structure involves (as foreseen by Szent-Gyorgyi ⁵⁾) some degree of general electronic delocalization ⁶⁾. This last situation arises from the fact that the peptide bonds, although separated from each other in the backbone by saturated carbons, are, however, united to each other by secondary cross linkages, namely hydrogen bonds. Inasmuch as these bonds may participate in electronic delocalization and transmit conjugation effects ⁷⁻⁹⁾, the existence of such a network represents the possibility of an extended electronic conjugation involving the whole molecular framework of the protein.

Nucleic acids, proteins, and energy-rich phosphates, although the most important representatives, are not the only conjugated constituents of the cells.

Pteridines, porphyrins, quinones, carotenoids, retinenes, melanins etc. . . . , are other important structural components of biomolecules belonging to the same type of conjugated compounds.

Another most striking observation in the same field concerns enzymes. There are hundreds of enzymes and they are essentially proteins. However, if one excepts the hydrolytic ones, most of the enzymes exert their catalytic activity in conjunction with a coenzyme. There is only a very limited number of essential coenzymes, about twenty, and practically all of these coenzymes are conjugated organic compounds. Such is the case, in particular, with the oxidation-reduction coenzymes, DPN, TPN, FAD, FMN, the haem prosthetic groups of the cytochromes, and the quinones. And it is also the case with the coenzymes involved in group transfer reactions: tetrahydrofolic acid, pyridoxal phosphate, thiamine pyrophosphate, vitamin B₁₂, etc. . . .

As a matter of fact, among the fundamental organic constituents of the living cell, carbohydrates, fats, and steroids seem to be the only non-conjugated type of molecules. Among these, carbohydrates and fats represent merely the fuel for the driving of the machinery without being functional constituents of it. The steroids generally possess a π -electron section, and, anyway, seem to be in some way involved in electron transfer phenomena^{10, 11}).

It is thus obvious that the basic manifestations of life are intimately connected with the existence of highly conjugated compounds, which for some decisive reason have been chosen by nature for being the vehicle of life.

When looking for such a reason one can hardly think of anything else than electronic delocalization which represents the most specific and at the same time the most important characteristic of such compounds. In what way can this outstanding feature of the resonating molecules account for their occurrence as the principle building stones of the living matter? We may distinguish at least two major factors responsible for this occurrence, related, respectively, to stability requirements and to functional advantages.

I. STABILITY

One of the major and most apparent results of electronic delocalization is the increment of stability which this delocalization confers on compounds in which it occurs. Quantitatively this increment is defined as resonance energy, and is nowadays one of the most familiar concepts of quantum chemistry. Particularly strong in pentagonal and hexagonal rings it may amount in the common previously quoted biochemicals from a few tens to a few hundreds of Kcal/mole (e.g. it is of the order of 30-45 Kcal/mole in the pyrimidines, of the order of 50-80 Kcal/mole in the purines and of the order of 200 Kcal/mole in the porphyrins). It represents an unexpected economy for the energy expenses in anabolic processes. Thus e.g. the de novo synthesis of purines from simple constituents may be considered as a series of ATP dependent synthesis of carbon-nitrogen bonds ¹²⁾. Eight such bonds are established during the formation of hypoxanthine, the first purine ring to be formed in this synthesis, and in every case but one the formation of such a bond is associated with the hydrolysis of an energy-rich bond of ATP. This represents an energy cost for the synthesis of the purine skeleton of about 50-60 Kcal/mole. The gain of resonance energy associated with this synthesis, calculated by the molecular orbital method ³⁾, is 3.4β which with $\beta = 16$ Kcal/mole represents about 55 Kcal/mole and compensates thus this expenditure.

It seems natural to assume that this thermodynamic stabilization must have played a non-negligible role in the evolutionary selection of this type of molecules for biochemical processes. It is widely acknowledged today ¹³⁻¹⁶⁾ that the biological evolution through the natural selection of species was preceded by a biochemical (or prebiological) evolution, a long period during which a great number of molecules and aggregates were formed, altered and destroyed and during which the molecules competed between themselves for reaction and function networks. This was the period of struggle for the survival and selection of biomolecules. Although the adaptability to the developing function was, of course, highly important it seems nevertheless that this condition must have been subordinated to the requirements of stability and that the molecules which finally gained must have been those which were the most stable and whose biochemical possibilities must have, in fact, oriented or at least influenced the function itself. A confirmation of this point of view may be found both in the extraordinary unity of biochemistry,

the same limited number of compounds being used all over the plant and animal kingdoms and in the multiplicity of functions linked with some of the basic skeletons. This last statement may be illustrated by two striking examples. The first one concerns the case of porphyrins. These very strongly resonance-stabilized molecules (in which four cyclic pyrroles are united by supplementary double bonds into a conjugated super-cycle) are utilized in photosynthesis, in the respiratory (electron transfer) enzymes and in the oxygen-carrying enzymes of higher animals. It seems as if nature having discovered this particularly stable skeleton has found means of utilizing it in a number of different functions. This point of view is substantiated by the observation that the chlorophyll molecule is today manufactured by a sequence of reactions almost identical with the sequence of reactions used to manufacture the heme. The branching between these two syntheses only occurs at the stage when the metal cation (ion or magnesium) is introduced into the porphyrin skeleton ^{15a)}. Following the authoritative opinion of Gaffron ¹⁷⁾ a number of other dyes could have been utilized with just as much efficiency as porphyrins in the photosynthetic apparatus. This author infers therefore that the porphyrins owe their predominant position essentially to the fact that they came first and were much more stable than other pigments. On the other hand ¹⁵⁾, Calvin has indicated strong reasons why, once the porphyrins formed, more of them will have a tendency to be formed by an autocatalytic self-selection mechanism due to the evolutionary pressure of peroxides.

The second example of polyfunction concerns the problem of adenine. This molecule seems to play an apparently unique role in nature. It is one of its most important single compounds and it enters into the constitution of a great number of complex biomolecules. Thus, adenine, besides contributing to the structure of the nucleic acid is also a part of several fundamental coenzymes (DPN, TPN, FAD, CoA) and other important transfer agents (S-adenosylmethionine), and it is also the carrier of the pyrophosphate chain in the energy-rich ATP and ADP. The clue to this omnipresence may perhaps reside in the fact that, as shown by calculations ^{18, 19)}, adenine has the greatest resonance energy among all the biochemical purines. It may not be unreasonable to imagine that, inasmuch as nature was induced to utilize a purine or pyrimidine base as a constituent of these fundamental biochemicals, a phenomenon of natural selection played a role, leading to the choice of the

energetically most stable base ^{*}).

Till now, we have considered the resonance stabilization of conjugated biomolecules as a thermodynamic advantage of their ground state. In fact, this stabilization seems to be equally effective in a second field in which its role must have been particularly important for the biochemical evolution. This second field concerns the effect of ionizing and ultraviolet radiations. As demonstrated in detail in the particular case of biochemical purines and pyrimidines, there is a very close parallelism between the resonance stabilization of biochemicals and their resistance to damage produced both by ionizing and ultraviolet radiations ^{21, 22}). The intimate nature of this correlation is not entirely elucidated but it seems highly probable that one of its predominant factors is the possibility for resonating molecules to produce under the influence of the radiation, relatively long-lived stable excited states. This possibility must have been particularly advantageous for the evolution of life under the early conditions of the earth in which the energy derived from the sun in terms of radiation or electronic discharges was the primary source of energy for the synthesis of molecules and even for the polymerization processes leading to macromolecules. The conjugated systems, whose loosely bound π and lone-pair electrons may be relatively easily raised to the excited states, were among those which could make the most efficient use of the available light energy ²³). It is possible that the $n \rightarrow \pi^*$ transitions of resonating heterocycles have been particularly advantageous in this respect, as they also seem to be nowadays in bioluminescence ²³). (We shall see later other reasons which point to the importance of the lone-pair electrons and of their participation in electronic delocalization for the processes of life). The involvement of resonating molecules, retinenes, as primary receivers of light in vision is, of course, self-explanatory. Less self-evident but no less significant is the involvement of retinenes also in the sense of smell ²⁴).

* This is, however, certainly not the only reason for the use of adenine, e.g. in coenzymes. In these compounds adenine probably serves for the binding between the coenzyme and the apoenzyme. An essential role in this binding seems to be played by the NH_2 group of adenine ²⁰). This is a very reactive amino group (more reactive than that of guanine or of cytosine) ^{18, 19}). A highly reactive group, fixed on a very resistant skeleton obviously represents a most successful combination for reactions involving this group. The same reason may be operating in ATP.

This same factor of stabilization through electronic delocalization might probably have played also a role in the evolutionary production of the huge macromolecular polymers, in particular nucleic acids and proteins. Such a formation is undoubtedly associated with complementary stabilization. As already mentioned the hydrogen bonds of proteins connect the otherwise isolated π -electron possessing peptide links into a one quasi-conjugated π electron system. A more quantitative observation concerns the complementary resonance stabilization through hydrogen bonding of the purine-pyrimidine pairs of the nucleic acids. Calculations have predicted that this stabilization should be by about 1 Kcal/mole greater for the guanine-cytosine pair than for the adenine-thymine pair²⁵⁾. This prediction is remarkably confirmed by experiment²⁶⁾ which indicates that the denaturation temperature of the nucleic acids rich in guanine-cytosine is appreciably higher than that of the nucleic acids rich in adenine-thymine. In fact, as far as our present knowledge goes, the purine-pyrimidine pairs which actually exist in DNA seem to be more stable than the artificial combinations recently created between other related polynucleotides²⁷⁾. In the nucleic acids there is probably moreover, besides the H-binding between the complementary purine-pyrimidine bases, the possibility of electronic interactions among the π electrons of the parallel stacked base-pairs, either by direct σ -type overlap of their electronic orbitals^{28,29)} or by a charge transfer complex formation between them^{30,31)}. Moreover, such surprising selection phenomena as the exclusive use of D-sugars in the nucleic acids and of L-amino acids in the proteins, correspond also to stability requirements, as it is only such a selection that permits the construction of regular helices with minimum strain¹⁶⁾.

Nevertheless, it seems certain that in fact this elaboration of biological macromolecules, which may be considered as the second important stage in the prebiological evolution (the first one being the selection of the appropriate conjugated molecules) offered also appreciable functional advantages over the use of smaller compounds³²⁾ and this situation brings us to the discussion of this second factor responsible for the evolutionary selection of conjugated molecules in biochemistry.

II. FUNCTIONAL ADVANTAGES

Life is a delicate, dynamic equilibrium between a series of synthesis and decomposition phenomena. Among its main characteristics are the constant mobility of its mechanisms, the interdependence of its constituent biochemicals, the long-range transmission of its manifestations and its numerous transducing activities. It appears obvious that the mobility, the fluidity, the great polarizability of the electronic cloud of conjugated molecules, the possibility that the existence of such a unique, large and deformable cloud offers for the rapid and distant transmission of perturbations (which in biological language may mean an order or a warning) represent important functional advantages which make the conjugated systems particularly suited to perform the functions required by the existence of the living matter. The essential fluidity of life agrees with the fluidity of the electronic structure of these compounds.

As mentioned before, a number of functional advantages may be found for the utilization of macromolecular polymers as the fundamental substances of life. Among those some are very explicitly related to the enhanced and extended electronic delocalization which occurs in such compounds.

Thus, although the exact nature of the semiconductivity observed in such polymers and in other organized solid state like biological structures^{6, 33)} is still uncertain (intrinsic electronic conductivity or extrinsic electronic conductivity or ionic conductivity), it nevertheless obviously represents a most interesting procedure for the long-range transmission of electronic perturbations. Inasmuch as catalysis by semiconductors involves the formation of charge transfer complexes between the catalyst and the substrate, the theoretically predicted decrease in ionization potential and increase in electron affinity of a protein chain with respect to these properties in an isolated peptide link may have an important significance for the catalytic activity of enzymic proteins^{3, 9)}.

In the very important field of bioenergetics, the utilization of the "energy-rich" phosphates as the principle coupling agents for the driving of anabolic reactions springs out from some advantageous characteristics of these compounds which, again, are due to the conjugation of their mobile electrons³⁴⁾. Thus, the principal sources of the "energy-wealth" of these phosphates are: 1) the resonance stabilization of the products of the hydrolysis, 2) the electrostatic repulsions due to the particular electronic distribution in the phosphates (consisting generally of a main chain of at

least three and frequently more atoms carrying net positive charges surrounded by a cloud of negatively charged atoms), distribution which is a direct result of the delocalization of the mobile electrons, 3) the keto-enol tautomerism of the products of the hydrolysis and 4) the free energies of ionization. The "energy-wealth" is therefore directly dependent on the manifestations of electronic delocalization.

However, the most striking example of the functional advantages associated with the utilization of conjugated molecules in the living systems is offered by the case of coenzymes. Biochemical reactions need enzymes to proceed and enzymes are essentially proteins. However, the great majority of enzymes exert their activity in conjunction with a coenzyme in which case the essential reaction takes place at the coenzyme, the function of the protein (or apoenzyme) consisting mainly in insuring the high efficiency and the specificity of the reaction, by suitably orienting and polarizing the reactants. Now, there are hundreds of enzymes but, as already mentioned, there is only a very limited number of coenzymes and, practically all of these coenzymes are conjugated organic molecules. This is in no way an accident but a deeply significant situation arising from the simple fact that these conjugated molecules are particularly well adapted for being the sites of biochemical transformations.

This may be illustrated by examples which we shall take in the field of two of the most important groups of coenzymes, the oxidation-reduction coenzymes and the group-transfer coenzymes.

Thus it has been shown ³⁵⁾ that the mechanism of functioning of the oxidation-reduction coenzymes (DPN, TPN, FMN, FAD, the haem prosthetic groups of cytochromes) in electron transfer may be related to the values of the energies of the lowest empty molecular orbital (lomo) of their oxidized form and of the highest occupied molecular orbital (homo) of their reduced form and to the variation of the energies of these two essential orbitals in the course of the oxidation-reduction. It is observed that, in each case, the oxidized form of the coenzyme has a very low-lying lomo and the reduced form of the coenzyme a particularly high-lying homo. The oxidation-reduction of these compounds is thus associated with an instantaneous redistribution of these two essential orbitals in such a way that in each case the oxidized form of the coenzyme has a relatively great electron affinity or electron-accepting tendency and the reduced form of the coenzyme a particularly low ionization potential or a particularly strong electron-

-donating tendency. This oscillation makes these coenzymes particularly suitable for being the vectors of electron transfer. Now, obviously, only conjugated molecules can involve such a specific displacement of molecular orbitals and satisfy the conditions imposed upon the efficient electron-transfer agents. In fact, even among the conjugated molecules themselves, only very specific ones can fulfill these requirements. Thus, e.g. if we replace the nicotinamide ring of the pyridine nucleotides by benzene or the isoalloxazine ring of the flavin coenzymes by anthracene, nothing useful will happen. This remark brings us to an essential complement to our general thesis about the importance of conjugated molecules in the processes of life. Namely, that what is needed and essential are not simply conjugated molecules but, mostly, conjugated heterocycles disposing of atoms with lone-pairs, such as nitrogen or oxygen, which by undergoing suitable changes in their valence-states are able to bring about the most economical and spectacular transformations. Thus the previously discussed redistribution of the molecular orbitals in the respiratory coenzymes, which apparently is so well adapted to the function of these coenzymes as electron transfer agents, is only possible because the oxidation-reduction is associated with changes in the valence state of the nitrogen atoms of these compounds, which alternatively involve their lone-pair in the overall π -delocalization or exclude it from such a participation. It may even be observed that owing to this modification in the valence state of the nitrogen atom the reduction of DPN^+ to DPNH does not involve any loss in the total number of the π -electrons of the system (in DPN^+ , N_1 contributes one π electron, while in DPNH it contributes its lone pair) and that the reduction of FMN to FMNH_2 involves even an increase in the total number of π electrons (in FMN , N_1 and N_{10} contribute one π electron each, in FMNH_2 , they contribute two electrons each, namely their lone pairs). Although the reduction is in each case accompanied by a certain loss of resonance energy ³⁶⁾, this loss is probably the minimum possible one.

Our second example comes from the field of group transfer coenzymes. We may specifically quote, as an illustration, the case of pyridoxal phosphate although exactly the same or very similar considerations apply to other coenzymes of this category such as thiamine pyrophosphate or tetrahydrofolic acid.

Pyridoxal phosphate, which is a heterocyclic aldehyde, catalyzes a great number of group transfer reactions involving the α -amino acids of the proteins ³⁷⁾. The mechanism of functioning involves, in the first place, the

formation of a Schiff's base (an imine) between pyridoxal phosphate and the α -amino acid. This formation labilizes the departure of the COOH^+ , H^+ , and R^+ groups attached to the α -carbon, permitting thus the involvement of the α -amino acid in a series of reactions. It may be shown that the essential electronic factors connected with the catalytic properties of pyridoxal phosphate reside in ^{38, 39};

1) the strong resonance stabilization of the transitional form deriving from the initial Schiff's base through the labilization of any of the COOH^+ or H^+ or R^+ groups, stabilization due to the increase in dimensions or the reorganization or both of the total conjugated system;

2) the creation in this transitional forms of prominent centers of extremely high reactivity (e.g. great local concentrations of electronic charges or of free valences), which insures the rapid consecutive development of the reaction towards its final products.

Thus the catalytic activity of this and similar coenzymes is essentially related to the transformation of the initial coenzyme-substrate complex into a resonance stabilized and, at the same time, electronically activated intermediate which is the essential active form of the reaction. Only conjugated molecules, with their cloud of mobile and deformable electrons and containing heteroatoms capable of oscillating between different valence states can bring about such results.

These different phenomena definitely seem to point out that there were deep reasons for the evolutionary choice by nature of conjugated molecules for biological purposes. We know, nowadays, owing to the work of a series of authors that all the essential biomolecules, in particular the amino-acids ^{15, 40, 41}) and even the fundamental purines ^{42, 43}) and pyrimidines ⁴⁴), could have been produced and probably were produced in the early stages of the history of the earth in a random, irregular, abiotic way. (An interesting point to investigate is to determine the probability factors or entropy contributions related to this formation. This unfortunately seems, at present, difficult for quantum chemistry). It seems highly probable that the evolutionary selection tended then towards the biological utilization of the most stable compounds which, not by chance but by the particular virtue of the π electrons, must have also been at the same time the most efficient and best adapted compounds for the biological purposes of nature. We cannot say and don't want to say that life has originated with the appearance of the conjugated compounds but what may probably be safely said is that the possibility of life, in the form in which

it is present today, has been rendered more probable and its development hastened through the utilization of such compounds. This truth is to some extent inherent in the very elementary chemical composition of the living matter ⁴⁵⁾: 99 o/o of it is composed of hydrogen, carbon, nitrogen and oxygen, the last three first-row elements being among all the elements those which most easily form multiple bonds. The next two most abundant and important elements to enter into the structure of the cell are sulfur and phosphorus and these are practically the only other than first-row elements to form multiple bonds. One can also imagine ⁴⁵⁾ that carbon rather than silicium has been chosen by nature as an essential component of organic matter (although silicium is much more abundant on the surface of the earth than carbon) possibly because carbon may form chains of conjugated double bonds while silicium cannot and possibly because carbon bonds are much stronger than silicium bonds. The choice and utilization of conjugated heterocycles as structural components of life appear, thus as one of the most important quantum effects in biochemical evolution.

III. RESONANCE AND BIOLOGICAL EVOLUTION

We have essentially considered till now the role of electronic delocalization or resonance in prebiological, chemical evolution. It may be pointed out that the same factor might have had also a decisive influence on the biological evolution of species ⁴⁶⁾. Thus, as it is well known the purine and pyrimidine bases of the nucleic acids are considered as existing essentially in the lactam and amino tautomeric forms. This situation is in agreement with quantum-mechanical calculations about the relative stabilities of the different possible tautomeric forms of the bases ³⁾. However, the involvement of rare tautomeric forms is considered as possibly playing an essential role in mutations ⁴⁷⁾. The presence of a rare tautomeric form may produce an erroneous coupling, through hydrogen bonds, of unusual bases and may lead to an induced, self-perpetuating, perturbed sequence of purine-pyrimidine bases. As the genetic information is probably enclosed in this sequence, the result is a mutation. The situation concerns in the first place spontaneous mutations whose occurrence appears as a physical necessity due to the mere existence of tautomeric equilibria and, secondly, to induced muta-

tions, produced e.g. by base analogs or antimetabolites capable of increasing the frequency of the abnormal pairings.

Now it can easily be shown ⁴⁶⁾ that one of the principal factors responsible for these tautomeric shifts towards rare forms and thus possibly responsible for the occurrence of mutations is a resonance effect. This is true in particular for spontaneous mutations. Thus, the essential varying factor responsible for the relative tendency of the bases to exist in a rare tautomeric form is the variation of the resonance energy which accompanies the tautomeric transformations. There are two such transformations to be considered: the lactam-lactim and the amino-imine transformations. In the lactam-lactim tautomerism, the transformation of the lactam form (the most stable) to the lactim form (less stable) is accompanied by an increase of resonance energy so that the proportion of the lactim form will be the greater, the greater this increase. In the amino-imine tautomerism, the transformation of the amino-form (the more stable) to the imino form (less stable) is accompanied by a decrease in resonance energy and will therefore be the greater, the smaller this decrease.

These considerations indicate clearly the predominant role of resonance energy variations in the production of spontaneous mutations and thus in the biological evolution. Explicit calculations carried out for the resonance energies of the different tautomeric forms of the purine and pyrimidine bases of the nucleic acids, lead moreover to the prediction, that the base which, from that point of view, should have the greatest tendency to exist in a rare form, either lactam or imino, is cytosine (a prediction which seems to be confirmed from the purely chemical point of view). As far as the starting hypothesis about the cause of spontaneous mutations is correct, it is the tautomerism of cytosine which may be expected to have the greatest probability of being involved in such mutations. Of course, from the practical point of view, it is evident that the electronic factor considered above cannot be the only one to play a role in this phenomenon. For instance, the steric adaptability of the rare tautomer into the general architecture of the nucleic acid may play an important part in determining its aptitude to subsist and to be involved in coupling, through hydrogen bonds, with complementary bases. Löwdin ⁴⁸⁾ has pointed out recently the possibly important contributions of the mutual stabilization of two rare tautomeric forms engaged in such complementary binding.

If we add that the same phenomenon of tautomeric shift and erroneous coupling may possibly be one of the causes of "aging" (considered as a continuous loss of genetic information and an accumulation of sequence errors) and also of "spontaneous" cancer, that induced mutations and perhaps also chemical carcinogenesis may be approached from a point of view very similar to the one just described, that important drugs, whether harmful or therapeutic, are frequently conjugated or at least partially conjugated compounds, in fact in majority of cases, heterocyclics ⁴⁹⁾, we clearly realize to what a decisive degree is life depending on the properties of the mobile electronic systems of resonating molecules. In a recent paper on biochemical evolution A. Rich ⁵⁰⁾ states that unfortunately "at the present time, we do not have any guide lines for our thinking, that is general concept about molecular evolution which may prove of utility in understanding and interpreting the results". We hope that the reasons indicated above for the orientation of life towards the utilization of conjugated systems, in particular O and N containing heterocyclics, may form such a concept.

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<p>Uppsala University, Sweden Quantum Chemistry Dept Rep. No. AD</p> <p>Contract: AF 61(052)-351 TN 86</p> <p>Monitoring Agency: USAF, EOOAR</p> <p>Field: Bioscience</p> <p>ELECTRONIC DELOCALIZATION AND BIOCHEMICAL EVOLUTION.</p> <p>Bernard Pullman and Alberte Pullman November 15, 62</p> <p>ABSTRACT: It is pointed out that most of the essential biomolecules which are related to or perform fundamental functions of living matter are constituted of completely or partially conjugated systems. The functional advances of such compounds in living matter are discussed.</p>	<p>Uppsala University, Sweden Quantum Chemistry Dept Rep. No. AD</p> <p>Contract: AF 61(052)-351 TN 86</p> <p>Monitoring Agency: USAF, EOOAR</p> <p>Field: Bioscience</p> <p>ELECTRONIC DELOCALIZATION AND BIOCHEMICAL EVOLUTION.</p> <p>Bernard Pullman and Alberte Pullman November 15, 62</p> <p>ABSTRACT: It is pointed out that most of the essential biomolecules which are related to or perform fundamental functions of living matter are constituted of completely or partially conjugated systems. The functional advances of such compounds in living matter are discussed.</p>
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